REMARKS/ARGUMENTS

The Pending Claims

Claims 35, 39-42, 45-48, and 50-53 are pending and are directed to a method of changing the sensory perception of an animal.

Discussion of Obviousness Rejection

Claims 35, 39, 40, 41, 42, 45-48, 50, 51, 52, and 53 remain rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,838,444 (Zoghbi et al. - "the Zoghbi patent") and U.S. Patent No. 5,837,511 (Falck-Pedersen et al. – "the Falck-Pedersen patent") alone, or in further view of U.S. Patent 6,821,775 (Kovesdi et al. - "the Kovesdi patent"), Staecker et al., *Otolaryngol. Head Neck Surg.*, *119*(1): 7-13 (1998) ("the Staecker reference"), U.S. Patent 6,455,314 (Wickham et al. - "the Wickham patent"), and/or Mizuguchi et al., *Gene Ther.*, *9*(12):769-776 (2002) ("the Mizuguchi reference"). Reconsideration of the objection and rejections is respectfully requested.

For subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467.

Consideration of the aforementioned Graham factors here indicates that the present invention, as defined by the pending claims, is unobvious in view of the cited references.

Regarding the scope and content of the prior art, the Zoghbi patent discloses a method of generating hair cells in an animal (e.g., a human) comprising delivering to the inner ear of the animal a nucleic acid encoding an atonal-associated factor using, for example, an

adenoviral vector. The Falck-Pedersen patent discloses methods for generating replication-deficient non-group C adenoviral vectors (i.e., subgroups A, B, D, E, and F).

The Kovesdi patent discloses an E1/E3/E4-deficient serotype 5 adenoviral vector encoding a pigment epithelium-derived factor (PEDF). The Staecker reference discloses a method of transfecting auditory hair cells with an HSV vector encoding brain-derived neurotrophic factor. The Wickham patent discloses recombinant adenovirus fiber proteins that are modified to reduce affinity for the CAR cellular receptor. The Mizuguchi reference discloses adenoviral vectors that are ablated for binding to CAR and αv-integrin, as well as adenoviral vectors containing the RGD peptide inserted into the HI loop of the fiber knob.

For the sake of argument and for purposes of the present analysis, one of ordinary skill in the art can be assumed to be someone with an advanced degree in a relevant field and a few years of experience in the relevant art.

As acknowledged by the Office Action, the Zoghbi patent does not disclose the use of a non-group C adenoviral vector comprising a nucleic acid sequence encoding Hath1. Moreover, the Zoghbi reference does not disclose or suggest the use of an adenoviral vector which comprises a nucleic acid sequence encoding Hath1 operably linked to a promoter that functions in supporting cells of the inner ear. The Office Action argues that the Zoghbi patent suggests using a promoter that functions in supporting cells because the Zoghbi patent cites a publication (Zine et al.) which allegedly discloses that the *Hes1* gene is expressed in developing cochlea of inner ears. The Zine reference discloses that the Hes1 and Hes5 genes are expressed in the developing mouse cochleae, with the Hes5 gene expressed in supporting cells. Neither the Zine reference nor the Zoghbi patent, however, discloses or suggests employing promoters which function in supporting cells of the inner ear to control gene expression of the Hath1 gene in an adenoviral vector.

The Falck-Pedersen reference does not disclose or suggest the use of an adenoviral vector which comprises a nucleic acid sequence encoding Hath1 operably linked to a promoter that functions in supporting cells of the inner ear.

None of the secondary references cited by the Office Action discloses or suggests an adenoviral vector which comprises a nucleic acid sequence encoding Hath1 operably linked

to a promoter that functions in supporting cells of the inner ear, much less a method of using such an adenoviral vector to change the sensory perception of an animal. Therefore, the cited references, even in combination, do not disclose or suggest the subject matter defined by the pending claims.

Furthermore, and contrary to the assertions of the Office Action, the claimed invention involves surprising and unexpected results. In this regard, Applicants submit herewith a second Declaration under 37 C.F.R. § 1.132 of Douglas E. Brough, which discusses experimental results that demonstrate that a subgroup D adenoviral vector (i.e., Ad28) encoding an atonal-associated gene operably linked to a promoter that specifically functions in supporting cells of the inner ear (i.e., GFAP promoter) improves vestibular function (i.e., changes the sensory perception) of injured mice.

The Office Action also states that it is "unclear why the declared 'enhanced' GFP expression by Ad35 or Ad28" (Office Action at page 11, first paragraph) that was demonstrated in the previous Rule 132 declaration is unexpected, given that non-subgroup C adenoviral vectors were developed to overcome technical difficulties associated with subgroup C adenoviral vectors (i.e., Ad5). As explained in the Rule 132 declaration submitted herewith, one of ordinary skill in the art would not have expected a non-subgroup C vector to transduce inner ear cells more efficiently than subgroup C vectors simply because it is not of subgroup C.

Considering all of the Graham factors together, particularly the fact that the combination of the cited references do not disclose all of the elements of the pending claims, and that the claimed invention involves surprising and unexpected results, it is clear that the present invention would not have been obvious to one of ordinary skill in the art at the relevant time in view of the combination of cited references. Accordingly, the obviousness rejections under Section 103 should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

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